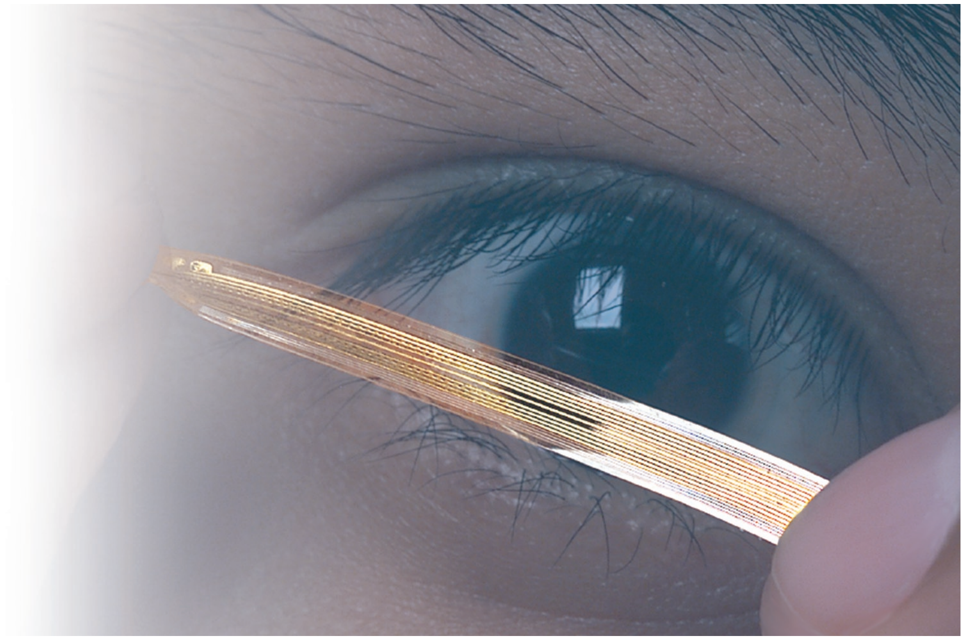
Retinal Prosthesis Provides Hope for Restoring Sight



A microelectrode array developed for a retinal prosthesis device. The electrodes are embedded in silicone-based substrate polydimethylsiloxane (PDMS). PDMS is a promising material for the microelectrode array, providing flexibility, robustness, and biocompatibility for long-term implantation.

VISION involves a complex process requiring numerous components of the human eye and brain to work together. When light enters the eye, nearly 127 million rods and cones, which are the photoreceptors in the retina, initiate a series of electrical signals so rapid that the images the eye receives appear to be continuously updated in a seamless process. A breakdown in this light-conversion process can lead to vision impairment or loss of sight.

A team of Lawrence Livermore engineers and scientists is participating in a national effort to develop a technology that would help restore sight to those who are legally blind from the loss of photoreceptor function. Attached to and functioning as the eye's retina, the retinal prosthesis device promises hope for those with age-related macular degeneration, retinitis pigmentosa, or related diseases where photoreceptors are damaged but the optic nerve and its connections to the brain are still intact.

The Department of Energy's Office of Science has committed $9 million over three years to retina research as part of the department's medical applications technology program. Courtney Davidson, electrical engineer and Livermore's lead on the project, is collaborating with colleagues from Oak Ridge, Argonne, Sandia, and Los Alamos national laboratories; the University of California (UC) at Santa Cruz; University of Southern California's (USC's) Doheny Eye Institute; North Carolina State University; and Second Sight, a private company that plans to commercialize the prosthetic device. The project is in its second year of funding.

Davidson and team members Satinderpall Pannu, Julie Hamilton, and Terri DeLima are part of Livermore's Center for Micro and Nanotechnology. The center is applying its expertise in the area of microelectromechanical systems (MEMS), which integrates millimeter-size mechanical elements, sensors, actuators, and electronics through microfabrication technology. The center's recent successes include developments in microfluidic filtration devices, microsensor technology with increased sensitivity, and micro fuel cells.

Davidson continues the work begun by his predecessors, engineers Peter Krulevitch and Mariam Maghribi, to develop an electrode array for the retinal prosthesis. The array will serve as the interface between an electronic imaging system and the eye, providing electrical stimulation normally generated by the photoreceptors that convert visual signals to electrical signals transmitted to the optic nerves. The goal is to develop a 4- by 4-millimeter array with 1,000 electrodes attached to a microchip system that powers them.

Designing Biocompatible Electronics

The electrode array is embedded in a silicone-based substrate, polydimethylsiloxane (PDMS). Livermore researchers previously used PDMS as a substrate for microfluidic tools in devices that collect and identify biological pathogens such as proteins, viruses, and bacteria. Additionally, Livermore efforts have focused on developing processes for embedding metal electrodes within PDMS for use in biomedical applications.

Davidson notes that PDMS is a biocompatible material, making it suitable for implants. While PDMS is somewhat permeable to oxygen, it is highly impermeable to water. This feature is expected to enable long-term implants where the electrodes must be isolated from corrosive and electrically conductive body fluids. The flexible nature of PDMS also allows the embedded electrodes to conform to the shape of the retina. Sandia and Livermore are each developing microfabrication processes and prototype electrode arrays in an effort to determine the best interface with the retina.

Mark Humayan, a retinal surgeon and biomedical engineer at USC's Doheny Eye Institute, is testing prototypes of the Livermore implants to determine how well the materials work and how long they are likely to last after implantation. Davidson says, "We've shown we can build electrode sets on PDMS, and we're looking at concepts that will increase the number of electrodes on a small area and allow a surgeon to test the device for conformability and robustness."

This past spring, surgeons at USC successfully implanted a prosthetic device in a dog's eye. The objectives were to determine how well the device conformed to the retina, the mechanical effects of the device on the retina, and any biocompatibility issues. Scanned images using optical coherence tomography showed the conformity of the implanted array on the retina. Surgeons were pleased with the results.

The device is designed to be epiretinal; that is, it will be placed on the surface of the retina inside the eye. The implant will overlap the center of the eye's visual field, which is the area affected in macular degeneration. Once implanted, a small camera attached to eyeglasses will capture a video signal that will be processed and transmitted inside the eye using a radio-frequency (rf) link. The rf link is composed of an external rf coil that will either be part of the eyeglass apparatus or will rest on the eyeball like a contact lens. Another rf coil inside the eye will pick up the signal and transmit it to electronics that will format the signal for stimulating the electrode array.

Powering Electrodes Inside the Eye

The power for the circuitry, or microchip system, will be provided inductively through transcutaneous coupling. That is, a coil attached to a battery on the side of the eyeglasses will inductively generate

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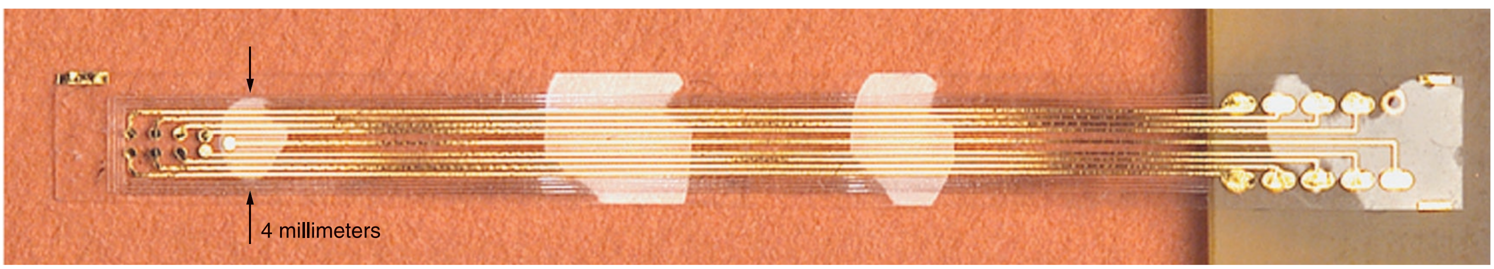

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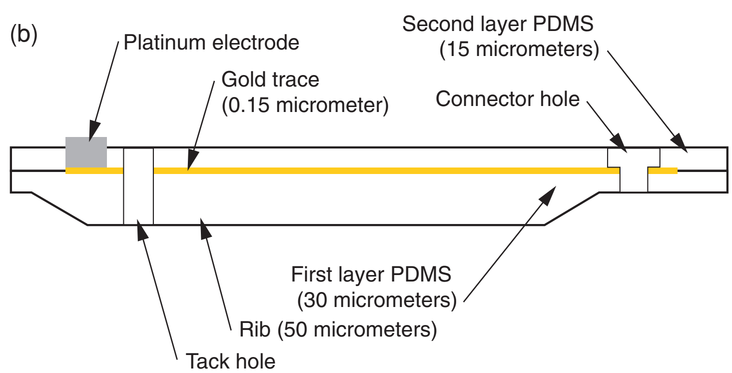
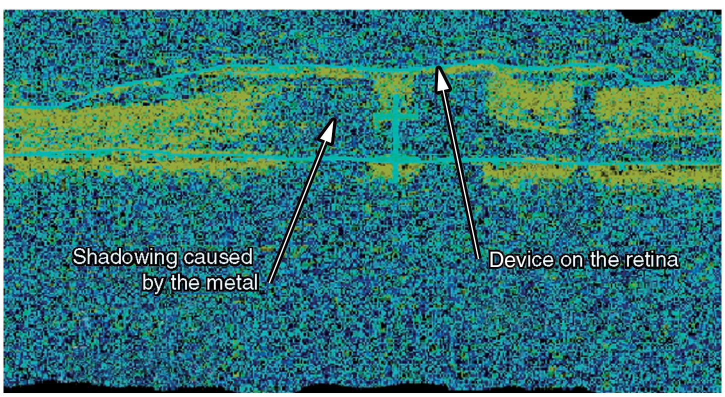


(a) Photograph of a prototype PDMS array used in testing.
(b) Cross-section of an eight-electrode polydimethylsiloxane (PDMS) device shows conductive lead and electrode metallization contained between two layers of PDMS. Reinforcement ribs facilitate handling of the thin PDMS device. A tack hole is used to pin the device to the retina.

power in a coil parallel to it under the skin. Wen Tai Liu, an engineer at UC Santa Cruz, is researching the requirements for the external camera and transmitter to determine the amount of power required by the implanted device and how best to supply the power.

North Carolina State University researcher Gianluca Lazzi is modeling the biological effects of retinal stimulation, notably, thermal dissipation. Davidson explains, "The electrodes must be stimulated in a very controlled manner. The amount of time you stimulate them and the amount of time given between the pulsing electrodes are critical. It's not certain what stimulation might be required to artificially generate normal vision. This is an extremely interesting area for both basic and clinical research." Los Alamos researcher John George is developing optical imaging techniques to observe the visual neural system and to better understand electrical stimulation of the retina.

Implanting electrical stimulation hardware within the fragile biological environment of the human eye poses challenges. Charged metal electrodes produce gases such as hydrogen and generate toxins that can damage tissues. Eli Greenbaum, project manager at Oak Ridge, is performing electrochemical tests of the electrodes to determine the limits before tissue damage. Second Sight is conducting experiments to determine the robustness of the device and producing prototypes. Argonne is developing an encapsulating package that will insulate the electronics to help assure that the implant will last a lifetime.



Optical coherence tomography scans taken one week after the prosthetic device is implanted in a dog's eye show it is conforming to the retina.

One challenge for the team is determining the best electrode metal for the array. Gold was a useful material for preliminary studies, but platinum has proven to be a better choice for biocompatibility. The questions now are what is the best design for the array and what method should be used to attach platinum to the PDMS substrate.

Another challenge is determining the correct density of electrodes. While a small number of electrodes may provide favorable results, the optimum density of electrodes is still to be established. The current operational goal is to produce 1,000 electrodes. An additional challenge is finding the best method to connect the microchip system to the electrode array.

A commercially available retinal prosthesis is at least a few years away. While the retinal project continues, Davidson is working on other potential applications of this technology. "Many parties are interested in collaborating with the Laboratory on other applications for the microarrays," he says. "For example, with just over a dozen electrodes in a prosthesis for hearing, you can get amazing results." In addition to a cochlear (hearing) implant, possibilities include a deep brain stimulation device for treating diseases such as Parkinson's and a spinal cord stimulation device for treating chronic pain.

Initially, the retinal device will rely on an external camera transmitter, but researchers hope to develop a complete implantable system. The Livermore team is encouraged with the results of the research that may help to restore eyesight to blind persons and may revolutionize the treatment for many neurologically based illnesses.

—Gabriele Rennie

Key Words: epiretinal, microarray, microfabrication, photoreceptor, polydimethylsiloxane (PDMS), retinal prosthesis.

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